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27. (amended) The method of claim 26, wherein said voltage pulse is comprised of a square wave pulse.

REMARKS

Claims 1-57 are currently pending. By way of this amendment, per the Examiner's suggestion, Applicant has changed the title of the application, canceled claims 1, 4, and 28-57 without prejudice, added new independent claim 58, and amended claims 2, 5-7, 17, 20, and 23-27. As a result, following entry of the amendment above, only claims 2, 3, 5-27, and 58 will be pending. Each of the foregoing amendments has been made to advance prosecution, and not for reasons of patentability. Accordingly, Applicants reserve the right to later prosecute claims equivalent to or more broad than the claims as they existed prior to the entry of the foregoing amendment in this or a related application.

Each of the claim amendments is supported by the specification and claims as originally filed, and do not include new matter. Specifically, original claim 1 has been replaced by new claim 58. Like claim 1, new claim 58 is directed to two-step methods of introducing agents into cells, although as specified in claim 58's preamble, the methods clearly involve electroporation. One step of the method involves injecting a therapeutic agent into a tissue of a patient in need of treatment. The other step concerns the use of an electrode apparatus to effect electroporation of the agent by delivering voltage pulses to establish electric fields sufficient to introduce the therapeutic agent into cells of the tissue. As specified in the claim, the electrode apparatus comprises a support member having disposed thereon two or more opposing pairs of needle electrodes arranged relative to one another to form an electrode array. Support for devices of this sort is found throughout the specification. For example, see Figure 2 and descriptions thereof. A "support member" is described at page 2, lines 1-4 of paragraph 0007. Pluralities of opposing pairs of needle electrodes are described at page 10, lines 2-4 of paragraph. At any given instant, some or all of the opposed pairs of needle electrodes may be energized by a power supply in electrical communication therewith.

The amendments to claims 2, 5-7, 17, 20, and 23-27 simply serve to ensure correct claim dependence and consistent use of terminology without extraneous language.

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Applicants respectfully submit that the claimed methods are both novel and non-obvious. For this reason, Applicants respectfully request reconsideration of the claims as amended in view of the following remarks.

a. Application Title.

The application's title has been objected to as not being descriptive of the claimed invention. Applicant herein has amended the title to reflect that the invention as claimed relates to methods of electroporation-mediated delivery of therapeutic agents, thereby mooting the basis of this objection. It may thus be withdrawn.

b. Double-patenting.

Claims 1-57 have been rejected under the judicially created doctrine of obviousness-type double patenting in view of U.S. patent no. 6,233,482. As acknowledged in the Office Action, that patent and the instant application are related, in addition to being assigned to the same entity. Moreover, given the priority dates of these related cases, they will by their nature expire simultaneously. Furthermore, the invention now claimed is not the same invention as that claimed in the '482 patent. For these reasons, Applicants respectfully submit that this rejection should be withdrawn.

c. 35 U.S.C. § 102 Rejections.

Claims 1-5, 7, 15-17, and 23-27 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. patent no. 5,674,267 (the "'267 patent"), and claims 1, 7, 8, 28-31, 34, and 35 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. patent no. 5,273,525 (the "'525 patent"). Applicant respectfully traverses each of these rejections as applied to now-pending claims 2, 3, 5, 7, 15-17, 23-27, and 58 because neither the '267 patent nor the '525 patent expressly or inherently disclose each and every element of the invention now claimed. Specifically, neither cited patent discloses an electrode apparatus having a support member on which is disposed two or more opposing pairs of needle electrodes arranged relative to one another to form an electrode array. Accordingly, the cited patents cannot anticipate electroporation methods that employ such devices. Since neither reference satisfies the applicable legal standard, these rejections should be withdrawn.

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d. 35 U.S.C. § 103 Rejections.

Claims 6, 18-22, 28-34, and 42-57 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable in view of the '267 patent, alone or in combination with the '525 patent. Applicant also respectfully traverses each of these rejections which, after entry of the amendment above, are understood to apply to now-pending claims 6, 9-14, and 18-22. The deficiencies of the cited art are discussed above, and it is clear that neither cited patent compensates for the shortcomings of the other with regard to the instant rejections. Because the cited patents, alone or in combination, neither teach nor suggest the methods as now claimed, Applicant respectfully submits that the instant 35 U.S.C. § 103 rejections should also be withdrawn.

CONCLUSION

Applicant respectfully contends that upon entry of the amendment above, the now-pending claims will be in condition for allowance. Applicant therefore earnestly solicits a notice to such effect. Should any issues or questions remain, to avoid the preparation of an additional official action and response thereto, the Examiner is encouraged to telephone the undersigned at 858.350.9690 so that the same may be promptly resolved.

Respectfully submitted,

Dated: 25 April 2003

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MARKED UP VERSION

AMENDMENT

A. In the Specification

- i. Please amend the title to read as follows:

[Improved Apparatus] Methods for Electroporation-Mediated Delivery for Drugs and Genes

- ii. At page 1, paragraph 0001, second line, please change "cell" to – cells --.

- iii. At page 13, paragraph 0060, first line, please change "particular" to -- particularly --.

B. In the Claims

- i. Please cancel claims 1, 4, and 28-57 without prejudice.

- ii. Please add new claim 58, as follows:

58. (New) A method of electroporating an agent into cells of a tissue, comprising:

- (c) injecting a therapeutic agent into a tissue of a patient in need of treatment; and
- (d) using an electrode apparatus placed in contact with the tissue to deliver voltage pulses that establish electric fields sufficient to introduce the therapeutic agent into cells of the tissue by way of electroporation, wherein the electrode apparatus comprises:
 - i. a support member having disposed thereon two or more opposing pairs of needle electrodes arranged relative to one another to form an electrode array; and
 - ii. a power supply in electrical communication with the pairs of needle electrodes disposed in the support member, wherein the power supply provides voltage

pulses to at least two of the opposing pairs of needle electrodes to effect electroporation.

iii. Please amend claims 2, 5-7, 17, 20, and 23-27 as follows:

2. (amended) The method of claim 58 [1], wherein the agent is injected either prior to, simultaneously with, or after step b.

5. (amended) The method of claim 58 [1], wherein the voltage pulses are applied simultaneously to the at least two opposing pairs of [said] needle electrodes [simultaneously, sufficient to cause electroporation, thereby introducing said agent into said cells].

6. (amended) The method of claim 58 [1], wherein said method is *in vivo*.

7. (amended) The method of claim 58 [1], wherein the agent is selected from the group consisting of drugs, nucleic acids, polynucleotides, chemotherapeutic agents, peptides, polypeptides, and antibodies.

17. (amended) The method of claim 58 [1], wherein the cell are tumor cells.

20. (amended) The method of claim 58 [1], wherein said tissue is mammalian.

23. (amended) The method of claim 58 [1], wherein the electric field is from about 10 V/cm to 2000 V/cm.

24. (amended) The method of claim 58 [1], wherein from [about] 1 to about 100 [electrical] voltage pulses are applied.

25. (amended) The method of claim 24 wherein [the electrical] each voltage pulse[s] [are] is from about 10 usec and 100 msec.

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26. (amended) The method of claim 58 [1], wherein [the electrical] each voltage pulse is selected from the group consisting of a square wave pulse, an exponential wave pulse, a unipolar oscillating wave form of limited duration, and a bipolar oscillating wave form of limited duration.

27. (amended) The method of claim 26, wherein said [electrical] voltage pulse is comprised of a square wave pulse.

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